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Viral-mediated gene delivery for in vivo circuit manipulation in neonatal mice

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An abbreviated version of this protocol was published in Science Advances in Jun 2020

GABAergic interneurons excite neonatal hippocampus in vivo

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Detailed protocol

Abstract

Understanding the cellular and circuit basis of early activity-dependent brain development is key to addressing basic and translational neuroscience questions. To achieve this goal, we need to manipulate the activity of specific neuronal subtypes while assaying activity *in vivo* – but this is a daunting task in newborn mice. The major bottleneck has been the technical difficulty of delivering, expressing, and utilizing activity manipulation tools in the fragile neonatal mouse. Adeno-associated viruses (AAV) are a common gene transfer system in adults but generally take several weeks to achieve high expression; thus, they have not been widely used for *in vivo* studies of very young animals. We have refined an AAV-mediated approach for optogenetic and chemogenetic tool delivery at early developmental stages. By injecting AAV into the mouse brain at postnatal day 0 (P0), our approach allows manipulation of neuronal subtypes in the cortex, thalamus, and hippocampus in un-anesthetized neonatal mice as early as P3. This protocol describes the general guideline of viral-mediated gene delivery for *in vivo* circuit manipulation in neonatal mice.

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